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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/031,092 | 01/11/2002 | Jolyon Jesty | 0974/1F828-US1 | 6018 |

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| EXAMINER | |
|---|---|
| VENCI, DAVID J | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1641 | |

DATE MAILED: 07/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/031,092 | JESTY ET AL. | |
| | Examiner | Art Unit | |
| | David J Venci | 1641 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *01/11/2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

### *Priority*

Preliminary amendment inserting priority data into specification is recognized.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 1-3 recite a method comprising "detecting the catalysis" of a prothrombinase. Alternatively, claims 1-3 recite a method comprising "detecting the catalysis" of a modified prothrombinase substrate. There is no support in the specification for either claim interpretation. Although the specification provides for an assay of thrombin chromogenic activity, the specification does not provide for an assay of prothrombinase activity or an assay of modified prothrombinase substrate (i.e. prothrombin) activity. Generally, detecting the "catalysis" of a protein or enzyme is defined as detecting the effect of said protein or enzyme (Stedman's Concise Medical Dictionary for the Health Professions, 3rd Ed.), which is not to be confused with detecting the *per se* protein or enzyme.

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The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention. It is not known what catalytic entity is to undergo or receive "detecting."

In claim 1, the term "associated" is vague and indefinite because a person of skill in the art would not know whether component substance(s) comprising a "prothrombinase," which may be both exogenous and endogenous to platelets, are necessary or sufficient to create an association with a platelet. Thus, a person of skill in the art would not know whether the prothrombinase, as a whole, is "associated" to the platelet.

Claims 1-3, 5-7, 13, and 15-16 are indefinite for the recitation of "modified prothrombinase substrate." It is not clear what noun the adjective "modified" modifies.

### *Claim Rejections - 35 USC § 102*

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5, 9-11, 13, 15, 17 and 19-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Szczeklik et al. 80 BLOOD 2006 (1992).

Szczeklik et al. describe a method for assaying the activation state (see Title, "Generation of Thrombin") of a platelet (see p. 2006, col. 2, GENERATION OF THROMBIN IN VITRO, "platelet-rich plasma") by measuring prothrombinase product (i.e. thrombin) generation (see p. 2006, col. 2, STUDY DESIGN, first sentence) comprising a modified prothrombinase substrate (see Abstract, last sentence). A prothrombinase is necessarily present in the platelet-rich plasma of Szczeklik et al., and would have been so recognized by a person of skill in the art.

With respect to claim 2, Szczeklik et al. describe detecting the production of modified thrombin (see p. 2006, col. 2, GENERATION OF THROMBIN IN VITRO, first sentence).

With respect to claim 3, Szczeklik et al. describe detecting thrombin catalytic activity (see pp. 2006-7, GENERATION OF THROMBIN IN VITRO, "amidolytic activity").

With respect to claims 4 and 19, Szczeklik et al. describe a method comprising a platelet (see p. 2006, col. 2, GENERATION OF THROMBIN IN VITRO, "platelet-rich plasma"). Factor Xa, Factor Va and PS:PC vesicle are necessarily present in the platelet-rich

plasma of Szczeklik et al., and would have been so recognized by a person of skill in the art.

With respect to claims 5 and 15, Szczeklik et al. describe an acetylated prothrombinase substrate (see Abstract, last sentence).

With respect to claim 13, Szczeklik et al. describe a modified prothrombinase substrate (see Abstract, last sentence) and a prothrombinase product assay (see pp. 2006-7, GENERATION OF THROMBIN IN VITRO, "amidolytic activity").

With respect to claims 9 and 10, Szczeklik et al. describe the detection of fibrin or fibrinogen (see pp. 2006-7, GENERATION OF THROMBIN IN VITRO, "fibrinogen clotting time").

With respect to claims 11, 14 and 17, Szczeklik et al. describe the detection of a peptide (see pp. 2006-7, GENERATION OF THROMBIN IN VITRO, "chromogenic substrate")

With respect to claim 20, Szczeklik et al. describe the use of water (see pp. 2007, col. 1, line 2, "saline"). Water is necessarily present in the saline of Szczeklik et al. and would be so recognized by a person of ordinary skill in the art.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 8 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Szczeklik et al. 80 BLOOD 2006 (1992) in view of Phizicky & Fields, 59 MICROBIOL. REV. 94 (1995) (relevant portions included).

Szczeklik et al. describe a method for assaying the activation state of a platelet as substantially described *supra*.

Szczeklik et al. do not describe the detection of modified thrombin via Western, ELISA, immunodiffusion, SPR, FPA, chromogenic peptide cleavage assay, or PAGE analysis.

However, Phizicky & Fields teach the use of surface plasmon resonance (See p. 114, columns 1-2, SURFACE PLASMON RESONANCE) in order to measuring protein concentration (See p. 114, column 2, lines 2-9)

Therefore, it would have been obvious for a person of ordinary skill in the art to combine the method for assaying the activation state of a platelet, as taught by Szczeklik et al., with the method of measuring protein concentration, as taught by Phizicky & Fields, because Phizicky & Fields describe the recent development of surface plasmon resonance measurements as a "minor revolution in biology" (See p. 114, column 1, lines 54-58).

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Claims 12, 14 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Szczeklik et al. 80 BLOOD 2006 (1992) in view of Mattler & Bang, 38 THROMB. HAEMOST. 776 (1977) (abstract only).

Szczeklik et al. describe a method for assaying the activation state of a platelet as substantially described *supra*.

Szczeklik et al. do not describe the detection of modified thrombin via cleavage of glycyl-L-prolyl-L-arginine peptide.

However, Mattler & Bang teach the use of Chromozym TH (See ABSTRACT, lines 1-6) as a chromogenic substrate in order to detect thrombin activity (See ABSTRACT, lines 6-8).

Therefore, it would have been obvious for a person of ordinary skill in the art to combine the method for assaying the activation state of a platelet, as taught by Szczeklik et al., with the use of Chromozym TH, as taught by Mattler & Bang, because Mattler & Bang teach the use of synthetic peptides mimicking amino acid sequences adjacent to proteolytic activation cleavage precursors of thrombin is a sensitive and specific tool applicable to kinetic and clinical use (See ABSTRACT, last sentence).

## *Conclusion*

No claims are allowed.

## *Allowable Subject Matter*

Claims 6-7 and 16 would be allowable if rewritten to overcome the rejections under 35 U.S.C. 112, first/second paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

The following is a statement of reasons for the indication of allowable subject matter:

> With respect to claim 6, the prior art teaches the chemical modification of both thrombin and prothrombin (e.g. Szczeklik et al. 80 BLOOD 2006 (1992)). However, the prior art does not appear to teach or suggest the specific chemical modification of either thrombin or prothrombin using

sulfo-N-succinimidyl acetate. Therefore, Applicants' assay for the activation state of a platelet requiring the chemical modification of prothrombin with sulfo-N-succinimidyl acetate appears to be free of the prior art.

With respect to claims 7 and 16, the prior art does not appear to teach or suggest the use of mutated thrombins or prothrombins in an assay for the activation state of a platelet.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J Venci whose telephone number is 571-272-2879. The examiner can normally be reached on 08:00 - 16:30 EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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06/28/04